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(54) Title: BONDING LAYERS FOR MEDICAL DEVICE SURFACE COATINGS

(57) Abstract

A medical device is coated with a thin coherent bond coat of acrylics, epoxies, acetals, ethylene copolymers, vinyl polymers, polymers containing hydroxyl, amine, carboxyl, amide, or other reactive groups, and copolymers thereof. Outer layers may be applied and remain adherent to the substrate in water for an extended period. The bond coat may comprise cross linkers such as urea resins, melamines, isocyanates, and phenolics. Preferred polymers include vinylpyrrolidone–vinyl acetate, styrene acrylic polymer, ethylene acrylic acid copolymer, carboxyl function acrylic polymer, hydroxyl function acrylic polymer, and acrylic dispersion polymer. The coatings may be applied to inert metal or plastic surfaces of medical devices such as needles, guide wires, catheters, surgical instruments, equipment for endoscopy, wires, stents, angioplasty balloons, wound drains, arteriovenous shunts, gastroenteric tubes, urethral inserts, laparoscopic equipment, pellets, and implants. Methods of coating and coating liquids are provided.

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BONDING LAYERS FOR MEDICAL DEVICE SURFACE COATINGS

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to an adhesive coating for a medical instrument. More specifically, the invention relates to polymer compositions which, when applied to an insertable medical device, provide for improved adhesion of a coating to the surface of the device, and related methods.

2. Related Art

Medical devices such as catheters or guide wires are inserted through trachea, blood vessels, urethra or other celoms or tissues, or through catheters or drainage tubes etc. Such devices are required to have a high degree of smoothness to assure introduction of such devices without causing trauma to tissue encountered during placement. These surfaces may be further enhanced by having lubricity for preventing injury or inflammation of mucous membrane which would be caused when the devices remain in the tissue. Other requirements for medical device surfaces have also been recognized.

In some instances, it is advantageous for medical device surfaces to have the capability of serving as a depot for various physiologically active substances such as anti-thrombogenic substances, anti-microbial substances, anti-neoplastic substances, genetic materials, hormones, living cellular materials and others. Anti-thrombogenic materials, such as complexes of heparin with quaternary ammonium compounds, are used on medical device surfaces to prevent formation of blood clots on the surface, which can form rapidly on vascular prostheses in vitro. Antimicrobial agents including penicillins, cephalosporins, fluoroquinolones, aminoglycocides, silver, compounds, phenol compounds, biguanides and others have been proposed for use in surface coatings to control nosocomial infections that often occur on surfaces of implanted prostheses, U.S. Patent 5, 069,899, U.S. Patent 5,525,348, and U.S. Patent 4,442,133.

The construction of devices such as guide wires and catheters presents special problems for insertion. Guide wires generally include coiled guide wires formed of stainless steel and monofilament guide which may have plastic materials such as polyurethanes,

polyamides, polyolefins, etc. extruded over them to provide a surface to which coatings can adhere, and to provide smoothness and uniformity of the surface.

Catheters typically consist of plastic tubes which may have a single lumen or multiple lumens. Catheters may have balloons fastened along the tube to obstruct a vessel or to fix the catheters in a desired position. Catheters may also have ports at the distal end, side ports along part of the length, or other mechanical features needed to accomplish the particular device mission. Catheters may consist of a continuous length of tubing, or may comprise two or more sections of tubing consisting of similar or dissimilar materials which are welded together in order to have different properties at different locations along the length of the device. Catheters may be tapered, both within a segment or by having segments of differing diameters. Typical material of which catheters are constructed include polyamides, polyurethanes, vinyls such as polyvinylchloride, polyesters, polyolefins, silicones, and others. Typical diameters range from less than one millimeter to more than 8 millimeters.

As typically encountered in inserting a catheter, at the predetermined site, the guide wire tip is inserted through a catheter up to its tip opening, the catheter with the guide wire is inserted into for example a blood vessel percutaneously, and the catheter is further inserted through the vessel by using the guide wire as a leading and supporting guide. These operations produce friction and abrasive forces that apply to the surfaces of the medical device. It is desirable for the frictional resistance between the catheter inner surface and the guide wire to be low. Relatively high friction between the catheter and the guide wire not only prevents the guide wire from being inserted through the catheter, but the guide wire from being easily moved through the catheter, making it difficult to carry out subtle indwelling operations at the destined vessel site. Sometimes the guide wire cannot be withdrawn from the catheter, rendering the catheter lumen unusable despite the completion of the indwelling operation.

To avoid such problems, attempts have been made in the prior art to apply low frictional resistance Teflon and silicone oil to the outer surface of guide wires. Application of silicone oil fails to retain lubricity because of immediate loss of silicone coatings. Frequent applications add to frictional resistance, also undesirably creating troubles as mentioned above.

There is thus the need for a catheter and guide wire having a lower frictional resistance surface which enables more subtle operation in a vessel and can be easily inserted and remain at the site where catheters are otherwise difficult to manage during placement.

Polyurethane coatings have been applied directly on metal surfaces. U.S. Patent 4,876,126. However, commercial versions of this technology require thick layers (60-80 microns thick) in order to perform adequately. In practice, the thick layer extends continuously around the coated metal substrate. These layers have good cohesive forces and thus appear to

be tightly bound on the metal surface, even though these layers do not necessarily have good adhesion to the metal surface. A disadvantage of such coatings is that because the polyurethane and other plastic layers are so thick, the metal diameter of the underlying wire must be correspondingly diminished. This is especially troublesome on the very fine wires such as those used in coronary angioplasty or neurointerventional catheterization procedures. These wires have OD's of about 0.010" (about 250 microns) and may have the majority of the diameter (about 120 to 170 microns) composed of plastic materials instead of metals. An alternate method is the use of low frictional materials such as polytetrafluoroethylene coatings which have lower friction than metals and most other plastic materials and which can be applied directly onto metallic substrates. Other materials such as high density polyethylene have been tried, but the coefficients of friction are not low enough for such materials. Oils have been applied, and the coefficients of friction are low. However, such treatments are transient because they wear off during use.

Hydrogel coatings are known to provide a lubricious surface for insertable devices. However, metals and certain plastic materials such as polyolefins, polyamides, silicones, polyesters and some others have inert surfaces and it is often difficult to achieve acceptable adhesion when applying surface coatings, including hydrogel coatings, over such surfaces.

Hydrogels can absorb several times their weight in water when placed in an aqueous environment. Usually, hydrogel layers are attached to hydrophobic sublayer(s) and there may be a great deal of penetration of the hydrogel polymer molecules into the hydrophobic sublayer(s). The polymer molecules of both layers are left in a state of inter-molecular mingling, especially in the region of the interface between the two layers. As a result of the inter-molecular mingling, water that is taken up in the hydrogel may find its way to the

intersection between the substrate and the hydrophobic coating layer. The adhesion between the hydrophobic layer and the substrate is usually jeopardized by the moisture, and adhesive failure usually results. This process of moisture-induced adhesive failure is greatly exacerbated when the coating layers are thin.

Thin hydrophobic layers containing cellulose esters and acrylic polymers may be coated directly on metal substrates, U.S. Patent 5,001,009. Hydrogel coatings may be applied directly over such layers. Such systems perform well on coil type guide wires, because the coating is able to gain additional adhesion by penetrating between the coil wires. However, such layers tend to allow too much moisture penetration resulting in deterioration of adhesive bonds when applied onto mandril style metal substrates.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide materials which can be applied within layers directly on medical device surfaces on which it is difficult to achieve coating adhesion, and which allow layers to be applied over them to enhance performance and biocompatibility of such devices. It is another object of the present invention to provide methods for preparing such medical instruments.

It is a further object of the present invention to provide guide wires, catheters, drainage tubes, feeding tubes, and other devices which are used in contact with human tissues and fluids, with surfaces that show enhanced biocompatability and may become very lubricious when contacted by body fluids. It is another object to provide such devices which contain substances which combat infections, blood clots, inflammation, and other disorders that may result from in vitro placement and use of such medical devices.

According to a first aspect of the present invention, there is provided a medical device comprising a substrate having a surface to be coated. The surface is characterized as being relatively inert and does not have reactive functional groups on the surface. A polymer coating which may be a single or mixed (hybrid) polymer layer is provided on the substrate surface which is strongly bonded to the substrate surface. The polymer layer on the device surface is such that other layers applied over it will be strongly bonded to such layer.

Substrates to which coatings according to the invention may be applied include metals such as stainless steel, nickel, gold, chrome, nickel titanium alloy, platinum and others;

plastics such as silicone, polyethylene, other polyolefins, polyesters, and others. Preferred devices include needles, guide wires, catheters, surgical instruments, equipment for endoscopy, wires, stents, angioplasty balloons, wound drains, arteriovenous shunts, gastroenteric tubes, urethral inserts, laparoscopic equipment, pellets, or implants. Particularly preferred embodiments include coated guide wires, particularly mandrel-type wires, catheters, drainage tubes, insulation in pacemaker leads, and smooth thin wires for coronary angioplasty or neurointervention or other procedures requiring a wire thickness of less than about 10-20 mils (250-500 microns).

According to a second aspect of the present invention, there are provided methods for preparing medical devices, comprising coating the medical device surface with a thin polymer layer of suitable composition such that the thin layer bonds well to the substrate surface, and such that succeeding coated layers will be strongly bonded to said thin polymer layer. The device is then coated with other layers designed to enhance performance and for biocompatibility of the medical device. Such layers may include medicated coatings which can serve as surface reservoirs for physiologically active agents to release efficacious concentrations of such agents near the device surface, hydrogel coatings to provide surface lubricity, color containing coatings, abrasion resistant coatings, combinations of one or more of the above, and other coatings intended to enhance the performance of the device.

This invention satisfies a long felt need for a thin well-bonded lubricious coating for indwelling medical devices. The invention succeeds where previous efforts at bonding surface layers to medical devices have failed, despite extensive efforts in a crowded and mature art. The invention eliminates the need for thick coatings, with enhanced performance. The materials and methods of the invention were not previously known or suggested, and their advantages were not previously appreciated. Further objectives and advantages that can be attained by the present invention will become apparent from the detailed description.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In describing preferred embodiments of the present invention illustrated in the drawings, specific terminology is employed for the sake of clarity. However, the invention is not intended to be limited to the specific terminology so selected, and it is to be understood that each specific element includes all technical equivalents which operate in a similar manner

to accomplish a similar purpose. Thin bond or tie coat layers according to the invention may be applied to difficult-to-bond-to substrates in order that other layers which cannot normally be bonded to such substrates may be satisfactorily bonded. The polymers of the invention are sufficiently resistant to degradation by solvents in succeeding layers that the coating does not lose adhesiveness when soaked in water and is impervious to water diffusion from the surface.

Classes of polymers which may be employed include acrylic polymers and copolymers based on monomers such as methylmethacrylate, butylmethacrylate, isobutylmethacrylate, ethylmethacrylate, methylacrylate, acrylic acid, styrene methacrylate, styrene acrylate, and others; vinyl polymers and copolymers such as polyvinylpyrrolidone, vinylpyrrolidone-vinylacetate copolymers, ethylene acrylic acid copolymers, epoxy polymers, and others. Exemplary commercial products that may be used in the invention include acrylics such as ARYLOID^{R} (Rohm & Haas) AT-63, AT-51, AT-81, WR-97; Polyvinylpyrrolidone polyvinyl acetate copolymers such as PVP/VA (GAF) E-335, E-635; ethylene acrylic acid copolymers such as PRIMACOR^{TM} (DOW) 5989, 5990; melamine resins such as CYMEL (CYTEC Industries) 303, 370, 380; epoxies such as EPON (Shell) 1001. Other appropriate polymers having the requisite characteristics will be apparent to persons of ordinary skill.

The polymers preferably, but not necessarily, contain reactive groups or points of reactivity such as hydroxyls, mono-, di- and tertiary amines, acids such as carboxyl, amides, or other groups which represent points of chemical reactivity. The polymers and points of chemical reactivity are able to form attractive forces such as hydrogen bonding toward the medical device surface, and also toward the coating layers to be applied over them. Such bonds are very strong, and prevent penetration of the top coat layer and water without requiring covalent or other ionic links between the device surfaces and the thin polymer tie coatings.

Polymers with reactive groups are preferred to help bond with substrates like metals. However, polymers lacking such groups such as acrylic or styrene polymers may also be used.

The reactive groups can also react to form a cross-linked matrix or help to form a cross-linked matrix. If desired, cross-linkers such as urea resins, melamines, isocyanates, phenolics, and others may be incorporated to cross-link the polymers of the invention with themselves, by reacting with the points of chemical reactivity on the polymer chains.

Alternatively, cross-linkers may react with themselves to form a cross-linked matrix in which the tie coat polymers are enmeshed, resulting in a solvent-resistant layer. Cross-linking within the thin polymeric tie coats (either between the principal polymers or around them) is useful in promoting effective adhesion by ensuring that the solvents used in succeeding coating layers do not attack and degrade the tie coat polymer layer excessively and by resisting water penetration. When the tie coat layers are subjected to excessive solvent attack the polymer tie coat layer may be diluted by the succeeding coating layer thereby degrading the adhesive bond between the tie coat layer and the medical device surface. Excessive water penetration can also degrade adhesion.

Coatings according to the invention may be prepared with polymers that lack points of reactivity, such as acrylic or styrene polymers or copolymers. Likewise, coatings may be made without cross-linking. However, with such coatings a greater tie coat thickness may be required or desirable than with layers made of polymers with points of reactivity and layers with cross-linking, in order to achieve a high degree of adhesion of succeeding layers according to the invention. For example, cross-linked coatings with polymers having reactive groups may be about two to about ten microns thick, in contrast with a coating as in Example 1, where a water-borne acrylic styrene copolymer is applied to metal, with a hydrogel layer on top, and a total thickness of about 30-40 microns.

The tie coat layers of the present invention are extremely durable, even when immersed in water for prolonged periods. As will be shown in examples, coatings on stainless steel can be soaked in water for months without losing adhesion, even when hydrogel layers are applied to the samples. Hydrogel layers typically absorb several times their weight in water and serve as a pathway for water diffusion into the layer (s) between the hydrogel layer and the medical device surface. Such exposure to water, especially for extended periods represents a considerable challenge to the tie coats of the present invention and the fact that they are able to endure such challenges without adhesive failure is a surprising result. The tie coat layers of the present invention are so thin, typically less than 5 microns, that the adhesiveness is all the more remarkable.

The coatings of the invention may be thin, on the order of .0002" - .0005" (5-12 microns), although it may be as thick as is desirable. Preferably, the coating is in the range of about 2 to about 100 microns, more preferably less than about 80 microns, or 60 microns,

and particularly preferred embodiments are less than about 15 microns thick. Bond coats of about 2 to about 10 microns are generally quite adequate. If the coating is thicker, it may cause other problems in certain applications where thinness is important.

A coating according to the invention may include a bond coat of about 5 microns and a two-layer hydrogel comprising a 5 micron base coat and a 5 micron top coat, with a total thickness of about 15 microns.

Examples of substrates and bond coat formulations that are effective with them are listed below. Many other combinations will be apparent to a person of ordinary skill following the teachings of the invention.

stainless steel:	epoxy resin; vinylpyrrolidone-vinyl acetate copolymer; styrene acrylic aqueous dispersion; ethylene acrylic acid copolymer plus melamine resin; ethylene acrylic acid copolymer plus melamine resin plus hydroxyl function acrylic polymer plus isocyanate polymer; carboxyl function acrylic polymer plus epoxy resin; acrylic dispersion polymer
polyethylene	ethylene acrylic acid copolymer plus melamine resin plus hydroxyl function acrylic polymer plus isocyanate polymer
silicone	ethylene acrylic acid copolymer plus melamine resin plus hydroxyl function acrylic polymer plus isocyanate polymer plus oxygen plasma
polyester	ethylene acrylic acid copolymer plus melamine resin plus hydroxyl function acrylic polymer plus isocyanate polymer
polyamide	oxygen plasma plus polyvinylbutynal

The coatings are coherent in that they form a continuous surface layer. When coated with a top coat, the resulting coatings are resistant to removal on prolonged soaking in aqueous fluids, and are adherent to a wide variety of substrates.

There are several useful tests of adhesion of coatings comprising the bond coat of the invention. Two of them are the dry adhesion tape test and the wet rub test. Uncovered tie coat coatings generally adhere well to a substrate, as do tie coat coatings with a base coat such as a cellulose ester layer, but problems frequently arise when a surface coating is applied, such as a hydrogel. Completed coatings according to the invention are able to endure immersion in water

for at least an hour and remain adhesive and resistant to removal by abrasion as indicated by the wet rub test, and, after drying, the tape test. This sets them apart from the prior art.

In the wet rub test, parallel cuts are made through the coating with a razor or knife. The coating is immersed in water for a predetermined period, such as an hour. A finger is then rubbed briskly across the cuts. Peel-back of the coating constitutes coating failure. In the dry adhesion test, adhesive tape is pressed firmly onto the coating, then peeled off briskly. Removal of the coating constitutes failure.

The coatings according to the invention may be applied to the surface of a biomedical device or other device with sufficient thickness and permanence to retain the coating's desirable qualities throughout the useful life of the coated device. They have sufficient thinness to be useful in many applications inappropriate for prior art coatings. The coatings of the invention are nonreactive with living tissue and are non-thrombogenic in blood.

The coatings may be applied by various techniques such as dip, spray, brush, wipe, or other methods known to those skilled in the art. The coating solutions have low viscosities, typically less than 100 CPS, and have good spreading properties. The coatings are baked at elevated temperatures, typically 50°C to 100°C, to drive off the organic solvents.

Gas plasma treatment may be done according to conventional methods. A vacuum is drawn, a gas such as oxygen or ammonia is allowed in, it is excited with Rf, and the surface is allowed to stay in contact with the resulting plasma for a sufficient time, such as 20 minutes, to put functional groups on the surface. Oxygen produces hydroxyl surface groups, and ammonia produces amine groups covalently bound to the polymer surface. Over time the groups tend to fold into the surface and become less reactive, so plasma-treated surfaces are best used fresh.

The coating systems described herein produce coatings that remain bonded in aqueous fluids on surfaces such as polyethylene, polypropylene, polyamide, polyester, silicone and metals such as stainless steel, platinum, gold, nickel, titanium, nickel-titanium alloys, chrome and other surfaces that are generally considered as presenting adherence problems. It may be necessary to treat some surfaces with gas plasma or other ionizing treatment to promote adhesion to the substrates. The following examples show some embodiments of how the invention can be used.

EXAMPLE 1

A stainless steel surface was brush coated with the following solution, and dried for 30 minutes at 85°C. Add in order, stir until dissolved.

Epoxy resin	5.55gm
Xylene	2.37gm
Tetrahydrofuran (THF)	62.08gm
Cyclohexanone	10.0gm
Ethanol	2.5gm
Vinylpyrrolidone-vinylacetate copolymer	2.5gm

The coating was tested for adhesion by cutting lines through it with a knife and then rubbing briskly across the cuts with a finger after the coating was immersed in water. No failure of adhesion (i.e. peel back) occurred after the wet rub test. Next, the coating dry adhesion was tested by pressing Universal Tape 83436 tape (United Stationers Supply, Co.) firmly onto the coating and peeling the tape off briskly. No coating should be removed by this test. This sample showed no adhesion failure on the tape test.

EXAMPLE 2

A styrene acrylic aqueous dispersion polymer (55% solids) was brush coated on a stainless steel surface, and dried for 30 minutes at 85°C. This coating showed excellent adhesion when tested according to example 1.

EXAMPLE 3

A sample as per example 2 was overcoated with a hydrogel composition consisting of:

Polyvinyl pyrrolidone (PVP)	9.4gm
Ethanol	136.1gm
Butyrolactone	30.6gm
0.0625% nitrocellulose in cyclohexanone	3.8gm

The coating was dried for 25 hours at 85°C. The coating passed the wet and dry adhesion tests according to example 1.

EXAMPLE 4

The following solution was brush coated on a stainless steel surface, and dried at 85°C for 2 hours.

5% (w/w) Ethylene acrylic acid copolymer in tetrahydrofuran (THF)	15gm
Cyclohexanone	2gm
Melamine resin	.24gm

Xylene	.23gm
Butanol	.07gm
Trichloroacetic acid	.1gm

This coating was dried for 15 hours at 85°C. The adhesion of the coating was tested according to example 1, and had good adhesion under both wet and dry conditions.

EXAMPLE 5

A sample as per example 4 was overcoated with the following solution and dried 2 hours at 85°C.

Nitrocellulose solution*	170.6gm
Cyclohexanone	88.0gm
Benzyl alcohol	48.0gm
10% (w/w) polyurethane in THF	86.0gm
Acrylic polymer with hydroxyl function	18.0gm
Melamine resin	4.5gm
Xylene	17.55gm
Butanol	4.95gm
Trichloracetic acid	0.5gm

*Nitrocellulose solution:

¼" RS Nitrocellulose	687gm
Butyl acetate	459gm
Toluene	360gm
Ethyl acetate	894gm
Camphor	132gm
Dibutylphthalate	180gm

Next the sample was overcoated with the following hydrogel solution and dried for four hours at 85°C.

PVP	9.4gm
Ethanol	136.1gm
Butyrolactone	30.6gm
0.0625% Nitrocellulose solution in cyclohexanone	3.8gm

The adhesion of the coatings was tested according to example 1 and had good adhesion under both wet and dry conditions. The sample had good wet lubricity. If the first coating was omitted the adhesion failed under the test condition.

EXAMPLE 6

The following solution was dip coated on a stainless steel wire and dried for 2 hours at 85°C.

5%(w/w) ethylene acrylic acid copolymer in THF	15gm
Cyclohexanone	4gm
Hydroxyl function acrylic polymer	.24gm
Melamine resin	.06gm
80% (w/w) isocyanate polymer in THF	.32gm
Trichloroacetic acid	.20gm

Next the sample was overcoated with the same two overcoating solutions per example 5. The adhesion was good when tested according to example 1 under wet and dry conditions. The sample continued to show good adhesion after soaking in water for more than 130 days. The coating had good wet lubricity.

EXAMPLE 7

Polyethylene tubing was exposed to oxygen plasma treatment. The PE tube was then coated with the same coatings as per example 6. The adhesion was good when tested according to example 1 under wet and dry conditions. The sample had good wet lubricity.

EXAMPLE 8

Polyethylene tubing was treated as in example 7, except that the middle coating just underneath the hydrogel consisted of:

¼" RS Nitrocellulose	2.89gm
Dibutylphthalate	1.1gm
Camphor	.8gm
Polyurethane	6.8gm
Cyclohexanone	28.3gm
Methylethylketone	1.6gm
Benzyl alcohol	7.1gm
THF	10.1gm
Ethylacetate	2.3gm
Ethanol	14.7gm
Isopropanol	5.5gm
Toluene	22.9gm
Butylacetate	1.3gm

The sample had good adhesion when tested according to example 1 under both wet and dry conditions, and had good wet lubricity.

EXAMPLE 9

Silicone tubing was treated as in example 8. The coating had good adhesion when tested according to example 1 under wet and dry conditions, and the coating had good wet lubricity.

EXAMPLE 10

Silicone tubing was exposed to oxygen plasma treatment by placing in an evacuated vessel and subjecting to alternate cycles of adding oxygen and cycling Rf power. Initially, oxygen is fed in at 550 ± 50 mTorr for 0.25 minutes. The oxygen is turned off, and the Rf power is turned on, with 450 ± 50 watts forward and ≤50 watts reverse, for 2 minutes. These two steps are repeated five times, with the remaining oxygen cycles lasting 2 minutes. The tie coat is typically applied to the plasma treated surface before degradation of the plasma treatment, within a day or two.

Next, the treated tubing was dip coated with the following solutions and dried one hour at 85°C.

Polyvinylbutyral	18.0gm
Ethanol	35.4gm
Xylene	34.9gm
Methylethyl ketone	43.4gm
Propylene glycol methyl ether acetate	48.9gm
Dipropylene glycol methyl ether acetate	9.0gm
Isobutyl acetate	1.89gm

This coating was overcoated with the same hydrogel as used in example 3. The coated sample had good adhesion when tested according to example 1 under both wet and dry conditions, and had good wet lubricity.

EXAMPLE 11

Stainless steel was coated with the following solution and dried 60 minutes at 85°C..

Polyvinyl butyral	9.00gm
Ethanol	17.70gm
Xylene	18.19gm
Methylethylketone	21.70gm
Propylene glycol methyl ether acetate	24.45gm
Dipropylene glycol methyl ether acetate	4.50gm
Isobutyl acetate	.90gm
Acrylic polymer with hydroxyl function	1.52gm
Melamine resin	.38gm
Butanol	.42gm

Next, the sample was overcoated with the last two coatings that were used to overcoat the first coating in example 5. The sample had good adhesion when tested according to example 1 under wet and dry conditions, and the sample had good lubricity.

EXAMPLE 12

A sample of polyester tubing was treated as per example 8. The sample had good adhesion when tested according to example 1 under wet and dry conditions, and the sample had good wet lubricity.

EXAMPLE 13

A stainless steel surface was dip coated with the following tie coat solution and dried 2 hours at 85°C.

Carboxyl function acrylic polymer	1.85gm
Aromatic 150	2.32gm
Butyl Cellosolve	.33gm
THF	3.55gm
Xylene	.13gm
Epoxy resin	.39gm

Next, the sample was overcoated with the same hydrogel coating as per example 3, and dried for 2 hours at 85°C. The sample had good adhesion when tested according to example 1 under wet and dry conditions, and had good lubricity.

EXAMPLE 14

A sample of stainless steel was dip coated with the same tie coat solution as used in example 1, and was then dried for 2 hours at 85°C. Next, the sample was overcoated with the last two coatings of example 5. The sample had good adhesion when tested according to Example 1 under wet and dry conditions, and the sample had good lubricity when wet.

EXAMPLE 15

A sample of stainless steel was dip coated with the following tie coat composition, and was dried for 2 hours at 85°C.

Water	8gm
10% Triton x 100 nonionic surfactant	.88gm
50% Acrylic dispersion polymer	18.8gm

Next, the sample was overcoated with the last two coatings of example 5. The sample had good adhesion when tested according to example 1 under wet and dry conditions, and the sample had good lubricity when wet.

EXAMPLE 16

A sample of PEBAX polyamide tubing was treated according to Example 10. The sample had good adhesion when tested according to Example 1 under wet and dry conditions, and had good wet lubricity.

EXAMPLE 17

A sample of Nylon 12 tubing was treated as in Example 16, except that no oxygen plasma treatment was used. The sample had good adhesion when tested according to Example 1 under wet and dry conditions, and had good wet lubricity.

The embodiments illustrated and discussed in this specification are intended only to teach those skilled in the art the best way known to the inventors to make and use the invention. Nothing in this specification should be considered as limiting the scope of the present invention. Modifications and variations of the above-described embodiments of the invention are possible without departing from the invention, as appreciated by those skilled in the art in light of the above teachings. It is therefore to be understood that, within the scope of the claims and their equivalents, the invention may be practiced otherwise than as specifically described.

WHAT IS CLAIMED IS:

1. An insertable medical device comprising a biocompatible surface coating on an inert surface of the device, the coating comprising a coherent bond coat layer with a thickness of between about 1 and about 100 microns, comprising a bonding polymer forming bonds with the inert surface of the device, and further comprising an outer layer that adheres to the bond coat layer, the coating remaining adherent to the surface and resistant to abrasion and to removal from the device by adhesive tape after soaking in water for an extended period.

2. A device according to claim 1, in which the bonding polymer is selected from the group consisting of acrylics, epoxies, acetals, ethylene copolymers, polymers containing hydroxyl, amine, carboxyl, amide, or other reactive groups, styrene acrylic polymer, ethylene acrylic acid copolymer, carboxyl function acrylic polymer, hydroxyl function acrylic polymer, acrylic dispersion polymers, copolymers based on methylmethacrylate, butylmethacrylate, isobutylmethacrylate, ethylmethacrylate, methylacrylate, ethylacrylate, acrylic acid, styrene methacrylate, and styrene acrylate, polyvinylpyrrolidone, vinylpyrrolidone-vinylacetate copolymers, other vinyl polymers and copolymers, ethylene acrylic acid copolymers, epoxy polymers, and copolymers thereof.

3. A device according to claim 1, wherein the polymer includes a reactive group.

4. A device according to claim 3, in which the bond coat further comprises a cross linker that interacts with the reactive groups on the polymer chains, the cross linker being selected from the group consisting of urea resins, melamines, isocyanates, epoxies, and phenolics.

5. A device according to claim 1, wherein the bonds comprise non-covalent bonds.

6. A device according to claim 1, in which the bond coat thickness is between about 1 and about 10 microns.

7. A device according to claim 1, in which the total coating thickness is less than about 40 microns.

8. A device according to claim 1, in which the inert surface comprises a material selected from the group consisting of stainless steel, nickel, gold, chrome, nickel titanium alloy, platinum, another metal, silicone, polyethylene, other polyolefins, polyesters, and other plastics.

9. A device according to claim 1, the medical device being selected from the group consisting of needles, guide wires, catheters, surgical instruments, equipment for endoscopy,

wires, stents, angioplasty balloons, wound drains, arteriovenous shunts, gastroenteric tubes, urethral inserts, laparoscopic equipment, pellets, and implants.

10. A method for coating a medical device having an inert surface comprising applying to the surface a coating liquid comprising a solvent and a bonding polymer selected to form an adherent bond coating on the surface, drying the liquid to form a thin coherent bond coating that adheres to the surface of the medical device, then applying an outer layer that adheres to the bond coating, the overall coating remaining adherent to the substrate and resistant to abrasion and removal by adhesive tape after soaking in water for an extended period.

11. A method according to claim 10 in which the outer layer comprises at least one of a lubricious coating, a medicated coating, a colored coating, an abrasion-resistant coating.

12. A method according to claim 10 in which the applying step comprises dipping, spraying, brushing, or wiping.

13. A method according to claim 10 further comprising pretreating the inert surface by gas plasma or other ionizing treatment before the applying step.

14. A method according to claim 10 further comprising heating the coating to at least about 50 ° C to drive off the solvent.

15. A coating liquid for applying a bond coat to a medical device having an inert surface, comprising a solvent and a polymer that bonds with the inert surface of the medical device, and further comprising an outer layer that adheres to the bond coat layer, the coating remaining adherent to the substrate and resistant to abrasion and removal by adhesive tape after soaking in water for an extended period.

16. The coating liquid of claim 15 further comprising a cross linker that interacts with reactive groups of the polymers.

17. The coating liquid of claim 15 wherein the cross linker is selected from the group consisting of urea resins, melamines, isocyanates, epoxies, and phenolics.

18. The coating liquid of claim 15 wherein the viscosity is less than about 100 cps.

19. The coating liquid of claim 15 wherein the solvent is selected from the group consisting of water, xylene, tetrahydrofuran, cyclohexanone, ethanol, butyrolactone, butanol, trichloroacetic acid, benzyl alcohol, isobutyl acetate, methyl ethyl ketone, Aromatic 150, butyl cellosolve, and toluene.

20. The coating liquid of claim 15 further comprising a surfactant.

21. A device according to claim 1, the bond coat layer and the outer layer having an interface where the components of the layers are interpenetrated.

22. A composition adapted for forming a biocompatible surface coating on an inert surface of a medical device, the composition comprising a biocompatible bonding polymer that bonds with the inert surface of the device to form a bond coat, the bonding polymer further being selected to adhere to an outer layer applied over the bond coat layer, the coating remaining adherent to the substrate and resistant to abrasion and removal by adhesive tape after soaking in water for an extended period.

23. In a biocompatible coating for an insertable medical device having an inert surface, the improvement comprising a coherent bond coat layer formed by a bonding polymer that bonds with the inert surface of the device, the bonding polymer further adhering to an outer layer applied over the bond coat layer, the coating remaining adherent to the substrate and resistant to abrasion and removal after soaking in water for an extended period.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61L29/00 A61L31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 13718 A (STERILIZATION TECHN SERV) 20 August 1992 see page 2, line 24 - page 3, line 30 see page 6, line 14 - line 17 see page 7, line 4 - line 13 see page 8, line 30 - page 9, line 19 ---	1-3,5, 8-16,18, 19,21-23
X	EP 0 379 156 A (UNION CARBIDE CHEM PLASTIC) 25 July 1990 see page 4, line 1 - line 13 see page 5, line 18 - line 26 see page 5, line 56 - line 58 --- -/--	1-3, 6-15,18, 22,23

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 July 1998	13/07/1998

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 5 620 738 A (FAN YOU L ET AL) 15 April 1997 see column 1, line 61 - column 2, line 67 see column 5, line 9 - column 6, line 53	1-3, 5-15, 18-20, 22,23

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Information on patent family members

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PCT/US 98/01531

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